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book reviews

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Biomolecular crystallography: principles, practice and applications to structural biology. By Bernhard Rupp. Pp. 808. Abingdon, New York: Garland Science, Taylor & Francis Group, 2010. Price (hardcover) USD 145.00. ISBN 9780815340812. ISBN-10 0815340818.

In 1971, when I was a postdoctoral researcher with Nobel Laureate Dorothy Hodgkin in Oxford, I was approached by David Phillips and Louise Johnson, asking for my assistance. It emerged that David had been asked to write a review on protein crystallography but, given the pressures on his time, he had not yet started. David suggested that Louise and I could write the review instead. I was of course flattered. I found myself enthusiastically agreeing but then nervously asking when the date for submission might be. David looked embarrassed and admitted that the submission date had recently passed but he was sure that the publishers would extend it a little. I desperately photocopied everything on protein crystallography that I could find in the library to take away with me on holiday – there was not much as the science was still young. Nevertheless, when Louise and I eventually put our contributions together, we found we had ten sections covering all of the aspects of the theory and practice of protein structure determination and analysis. We sent it to the publisher, who very quickly replied that he would publish the summary section as the review, and suggested that we might put the other sections together as a monograph. This we did and five years later it became *Protein Crystallography* published by Academic Press.

Over the past 34 years Louise and I have often discussed the possibility of updating our text. Indeed at one time second-hand copies were selling at $1300 on EBay I am told. However, the number of papers on protein crystallography published in the past 35 years and the complexity of the subject were a huge challenge and we never quite rose to that. However, this marvelous text by Bernhard Rupp provides everything that we could have done and more: indeed all that is required for the student of 2010.

Biomolecular Crystallography is an impressive volume. Its 808 pages are beautifully written and wonderfully illustrated, many in colour. It begins with a discussion of proteins and nucleic acids, their structures, the challenges of crystallization and the opportunities for engineering proteins to encourage crystallization. It then moves on to describe the fundamentals of crystallography, the basis of crystal geometry and the origins of X-ray diffraction. This is done rigorously without avoiding mathematical descriptors of symmetry and diffraction. Indeed Bernhard Rupp presents a thoughtful analysis of statistics and their relevance to accuracy, discussing probability distributions, maximum likelihood and Bayesian inference. I am impressed that he has done this rather than compromising just with analogies, however valuable these undoubtedly are. Although macromolecular crystallographers these days tend increasingly not to be physicists or mathematicians, it remains important to understand the basics. The numbers of incorrect structures that are beginning to appear by mistake, and even by design, are evidence of this. *Biomolecular Crystallography* then goes on to discuss instrumentation and data collection, before reviewing calculation of electron density and solving the phase problem. These topics are all dealt with clearly but rigorously. The methodology is pretty well up to date and the approaches described reflect current best practice. The volume finishes with a useful discussion of the validation of protein structures. This is an all too important area and one that is often ignored. Although most approaches use knowledge of protein structures already determined, they can identify structures where there is something new or something wrong. All crystallographers simply need to know about this.

Bernhard Rupp's textbook has some very interesting and helpful features. Each chapter has a list of key concepts and additional reading, including very extensive and comprehensive references. There is a nice section on the presentation of structures for publication and a final appendix on the details of coordinate file formats, basic linear algebra, crystallographic coordinate systems and so on. There is a useful glossary with many terms concisely described and a very comprehensive index – all that one would want of a good text!

There is one obvious omission, the lack of an historical introduction. Macromolecular crystallography has been very much a family affair with researchers mapping their scientific ancestry to Bernal, Bragg, Lipscomb, Perutz, Hodgkin and so on. However, as Bernhard Rupp writes, this has been discussed many times, particularly well in the brilliant biographies of Bernal, Hodgkin and Perutz, as well as in the review of the origins of protein crystallography by Richard Dickerson. I think that this omission is justified. A more significant challenge for a present day author is to cover the extension of crystallography to cover polysaccharides, nucleic acids and large protein–nucleic acid complexes. Indeed ribosomes – the topic of last year's Nobel Prize – hardly get a mention, and viruses only a passing comment, but then the book is rather long already!

The applications of crystallography to structural biology in particular and to cell and molecular biology more generally are huge. Every good university now has structural biologists who use X-ray crystallography, NMR, electron microscopy and the many other techniques to inform us about the structure and organization of living matter at the molecular level. This book will be an essential part of the library of any

department that claims to make contributions to modern biology. Biomolecular crystallography is also helpful in underpinning structure-guided drug discovery. Although there was much scepticism about rational design in the 1970s and 1980s, most candidate molecules developed for therapeutic use are now subjected to structural analysis during lead optimization. There are also more recent developments in using high-throughput crystallography for screening fragments and for growing them into drug candidates. This is evidence that structural biology has real contributions to play in medicine, as well as in our general understanding of living organisms; it makes *Biomolecular Crystallography* a necessary addition also to the libraries of big pharmaceutical companies and small biotechs. This is a book to be enjoyed by all who wish to become structural biologists. I am also sure that many practicing structural biologists – even some who consider themselves mature – would do well to read its pages.

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